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     FILE 'REGISTRY' ENTERED AT 11:34:57 ON 29 OCT 1999
L1                STRUCTURE UPLOADED
L2              0 S L1
L3                STRUCTURE UPLOADED
L4              0 S L3
L5                STRUCTURE UPLOADED
L6              1 S L5
L7             40 S L5 SSS FULL

     FILE 'CAPLUS' ENTERED AT 11:38:23 ON 29 OCT 1999
L8             10 S L7
                  S L3

     FILE 'REGISTRY' ENTERED AT 11:38:42 ON 29 OCT 1999
L9              0 S L3

     FILE 'CAPLUS' ENTERED AT 11:38:45 ON 29 OCT 1999
L10             0 S L9

     FILE 'BEILSTEIN' ENTERED AT 11:40:55 ON 29 OCT 1999
L11             3 S L5
L12             0 S L3
L13             8 S L3 SSS FULL

=> d 13

L3 HAS NO ANSWERS
L3                STR
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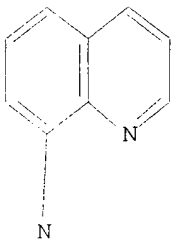

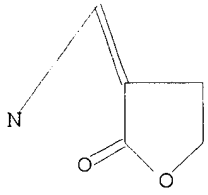


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Structure attributes must be viewed using STN Express query preparation.


=> d 15

L5 HAS NO ANSWERS
L5                STR
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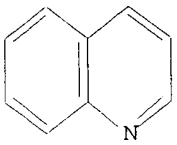
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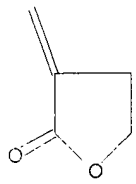

O
O

L13 ANSWER 1 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 3789555 Beilstein
Molecular Formula (MF): C19 H23 N3 O3 . (x) Cl H
Lin. Struct. Formula (LSF): C19H23N3O3*(x)HCl
Chemical Name (CN): 3-(1-<2-(6-methoxy-<8>quinolylamino)-ethylamino>-ethylidene)-5-methyl-dihydro-furan-2-one; hydrochloride
3-(1-<2-(6-Methoxy-<8>chinolylamino)-aethylamino>-aethyliden)-5-methyl-dihydro-furan-2-on; Hydrochlorid
Beilstein Reference (SO): 4-22-00-05782
General Comments (NTE): Stereo compound

Component Data:

Component Reg. No. (CBRN)	Component Molec. Formula (CMF)	Formula Weight (FW)	Lawson Number (LN)
3697002	C19 H23 N3 O3	341.41	27629, 20580, 3018, 289
1098214	Cl H	36.46	

CM 1

CBRN 3697002
CMF C19 H23 N3 O3

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
Atom/Bond Notes:
1. CIP Descriptor: E

CM 2

CBRN 1098214
CMF Cl H

=> d 2-3 ide pre

L13 ANSWER 2 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 344426 Beilstein
Molecular Formula (MF): C22 H29 N3 O3
Chemical Name (CN): 3-(1-<5-(6-methoxy-<8>quinolylamino)-pentylamino>-ethylidene)-5-methyl-dihydro-furan-2-one
3-(1-<5-(6-Methoxy-<8>chinolylamino)-pentylamino>-aethyliden)-5-methyl-dihydro-furan-2-on

Autonom Name (AUN):
3-(1-<5-(6-methoxy-quinolin-8-ylamino)-pentylamino>-
ethylidene)-5-methyl-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05816
Formula Weight (FW): 383.49
Lawson Number (LN): 27629; 20580; 3045; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: (+-)-3-acetyl-5-methyl-dihydro-furan-2-one, N-<6-methoxy-
<8>quinolyl>-petanediyldiamine
Temp: 150.0 Cel
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471, 473
2. Patent: Winthrop Chem. Co., US 2187847 1936
Note(s):
3. Handbook Data

L13 ANSWER 3 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 341112 Beilstein
Molecular Formula (MF): C21 H27 N3 O3
Chemical Name (CN): 3-(1-<4-(6-methoxy-<8>quinolylamino)-butylamino>-
propylidene)-dihydro-furan-2-one
3-(1-<4-(6-Methoxy-<8>chinolylamino)-butylamino>-
propyliden)-dihydro-furan-2-on
Autonom Name (AUN):
3-(1-<4-(6-methoxy-quinolin-8-ylamino)-butylamino>-
propylidene)-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05807
Formula Weight (FW): 369.46
Lawson Number (LN): 27629; 20579; 3036; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: BRN=117709 3-propionyl-dihydro-furan-2-one, BRN=185478
N-<6-methoxy-<8>quinolyl>-butanediyldiamine
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471
2. Patent: Winthrop Chem. Co., US 2187847 1936
Note(s):
3. Handbook Data

=> d 4-8 ide pre

L13 ANSWER 4 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 341102 Beilstein
Molecular Formula (MF): C21 H27 N3 O3
Chemical Name (CN): 3-(1-<4-(6-methoxy-<8>quinolylamino)-butylamino>-ethylidene)-5-methyl-dihydro-furan-2-one
3-(1-<4-(6-Methoxy-<8>chinolylamino)-butylamino>-aethyliden)-5-methyl-dihydro-furan-2-on
Autonom Name (AUN):
3-(1-<4-(6-methoxy-quinolin-8-ylamino)-butylamino>-ethylidene)-5-methyl-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05807
Formula Weight (FW): 369.46
Lawson Number (LN): 27629; 20580; 3036; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: (+-)-3-acetyl-5-methyl-dihydro-furan-2-one, BRN=185478
N-<6-methoxy-<8>quinolyl>-butanediyldiamine
Temp: 150.0 Cel
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471
2. Patent: Winthrop Chem. Co., US 2187847 1936
Note(s):
3. Handbook Data

L13 ANSWER 5 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 335331 Beilstein
Molecular Formula (MF): C20 H25 N3 O3
Chemical Name (CN): 3-(1-<4-(6-methoxy-<8>quinolylamino)-butylamino>-ethylidene)-dihydro-furan-2-one
3-(1-<4-(6-Methoxy-<8>chinolylamino)-butylamino>-aethyliden)-dihydro-furan-2-on
Autonom Name (AUN):
3-(1-<4-(6-methoxy-quinolin-8-ylamino)-butylamino>-ethylidene)-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05807
Formula Weight (FW): 355.44
Lawson Number (LN): 27629; 20578; 3036; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: BRN=112676 3-acetyl-dihydro-furan-2-one, BRN=185478
N-<6-methoxy-<8>quinolyl>-butanediyldiamine
Temp: 150.0 Cel
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471
2. Patent: Winthrop. Chem. Co., US 2187847 1936
Note(s):
3. Handbook Data

L13 ANSWER 6 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 331194 Beilstein
Molecular Formula (MF): C19 H23 N3 O3
Chemical Name (CN): 3-(1-<3-(6-methoxy-<8>quinolylamino)-propylamino>-ethylidene)-dihydro-furan-2-one
3-(1-<3-(6-Methoxy-<8>chinolylamino)-propylamino>-aethyliden)-dihydro-furan-2-on
Autonom Name (AUN):
3-(1-<3-(6-methoxy-quinolin-8-ylamino)-propylamino>-ethylidene)-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05797
Formula Weight (FW): 341.41
Lawson Number (LN): 27629; 20578; 3027; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: BRN=177341 N-<6-methoxy-<8>quinolyl>-propanediyldiamine,
BRN=112676 3-acetyl-dihydro-furan-2-one
Temp: 150.0 Cel
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471
2. Patent: Winthrop Chem. Co., US 2187847 1936
Note(s):
3. Handbook Data

L13 ANSWER 7 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 328034 Beilstein
Molecular Formula (MF): C19 H23 N3 O3
Chemical Name (CN): 3-(1-<2-(6-methoxy-<8>quinolylamino)-ethylamino>-ethylidene)-5-methyl-dihydro-furan-2-one
3-(1-<2-(6-Methoxy-<8>chinolylamino)-aethylamino>-aethyliden)-5-methyl-dihydro-furan-2-on
Autonom Name (AUN):
3-(1-<2-(6-methoxy-quinolin-8-ylamino)-ethylamino>-ethylidene)-5-methyl-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05782
Formula Weight (FW): 341.41
Lawson Number (LN): 27629; 20580; 3018; 289

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: BRN=163375 N-<6-methoxy-<8>quinolyl>-ethylenediamine,
(+-)-3-acetyl-5-methyl-dihydro-furan-2-one
Temp: 150.0 Cel
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471
2. Patent: Winthrop. Chem. Co., US 2187847 1936

Note(s):
3. Handbook Data

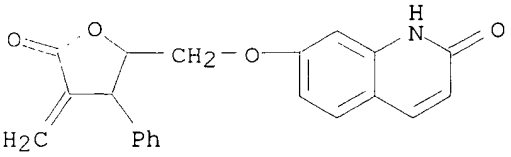
L13 ANSWER 8 OF 8 BEILSTEIN COPYRIGHT 1999 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 320348 Beilstein
Molecular Formula (MF): C18 H21 N3 O3
Chemical Name (CN): 3-(1-<2-(6-methoxy-<8>quinolylamino)-ethylamino>-ethylidene)-dihydro-furan-2-one
3-(1-<2-(6-Methoxy-<8>chinolylamino)-aethylamino>-aethyliden)-dihydro-furan-2-on
Autonom Name (AUN):
3-(1-<2-(6-methoxy-quinolin-8-ylamino)-ethylamino>-ethylidene)-dihydro-furan-2-one
Beilstein Reference (SO): 4-22-00-05781
Formula Weight (FW): 327.38
Lawson Number (LN): 27629; 20578; 3018; 289

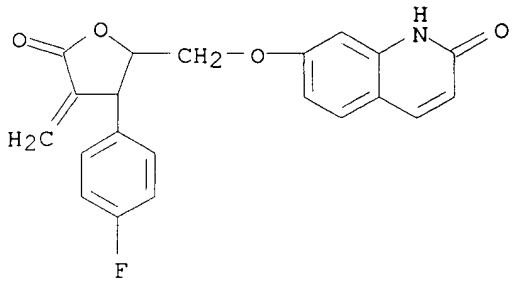
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Preparation:
PRE
Start: BRN=163375 N-<6-methoxy-<8>quinolyl>-ethylenediamine, BRN=112676 3-acetyl-dihydro-furan-2-one
Reag: ethanol
Temp: 130.0 Cel
Reference(s):
1. Patent: I.G. Farbenind., D.R.P. 663375 1935
Friedlaender, 23 471
2. Patent: Winthrop Chem. Co., US 2187847 1936
Note(s):
3. Handbook Data

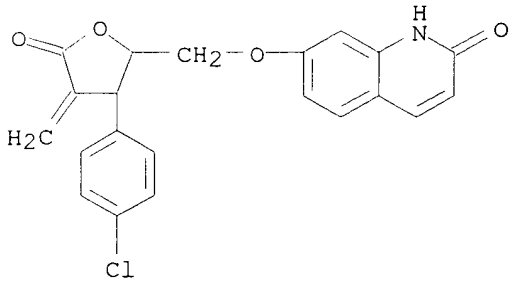
L8 ANSWER 1 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1999:29554 CAPLUS
DN 130:168226
TI Synthesis of certain quinolin-2(1H)-one .alpha.-methylene .gamma.-butyrolactones as potential antiplatelet agents
AU Chen, Yeh-Long; Wang, Tai-Chi; Fang, Kuo-Chang; Chang, Nein-Chen; Tzeng, Cherng-Chyi
CS School of Chemistry, Kaohsiung Medical College, Kaohsiung, Taiwan, Peop. Rep. China
SO Heterocycles (1999), 50(1), 453-462
CODEN: HTCYAM; ISSN: 0385-5414
PB Japan Institute of Heterocyclic Chemistry
DT Journal
LA English
AB Certain quinolin-2(1H)-one derivs. with various .alpha.-methylene-.gamma.-butyrolactones substituted at the C(7)-position were synthesized and evaluated for their antiplatelet activity against arachidonic acid (AA)-, and platelet-activating factor (PAF)-induced aggregation in washed rabbit platelets. 7-Hydroxyquinoline 1-oxide was treated with acetic anhydride followed by the hydrolysis of 1.0 N NaOH to afford 7-hydroxyquinolin-2(1H)-one. The desired 7-[(2,3,4,5-tetrahydro-4-methylene-5-oxo-2-furanyl)methoxy]-quinolin-2(1H)-ones were obtained from the latter via alkylation and the Reformatskii-type condensation. These quinolin-2(1H)-ones were approx. five to seven times more potent than their coumarin counterparts against AA- and PAF-induced aggregation and are approx. two hundred times more potent than aspirin against AA-induced aggregation.
IT **220365-05-9P 220365-06-0P 220365-07-1P 220365-08-2P 220365-09-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of .alpha.-methylene-.gamma.-butyrolactone-substituted quinolinones as antiplatelet agents)
RN 220365-05-9 CAPLUS
CN 2(1H)-Quinolinone, 7-[(tetrahydro-4-methylene-5-oxo-3-phenyl-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



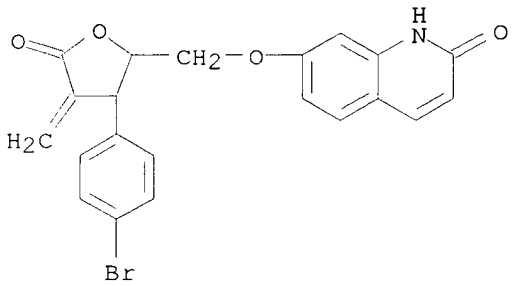
RN 220365-06-0 CAPLUS
CN 2(1H)-Quinolinone, 7-[[3-(4-fluorophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



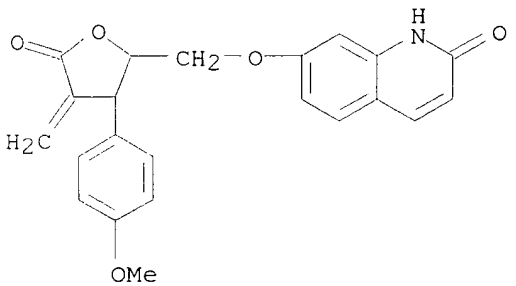
RN 220365-07-1 CAPLUS
CN 2(1H)-Quinolinone, 7-[[3-(4-chlorophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



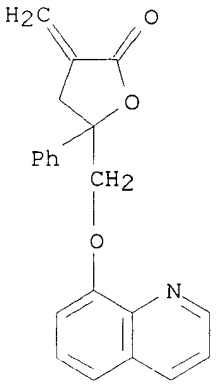
RN 220365-08-2 CAPLUS
CN 2(1H)-Quinolinone, 7-[[3-(4-bromophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



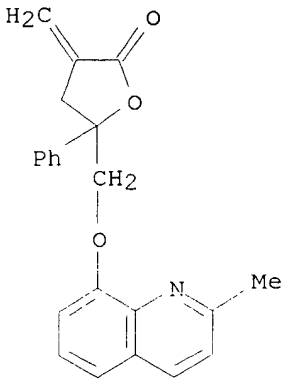
RN 220365-09-3 CAPLUS
CN 2(1H)-Quinolinone,
7-[[tetrahydro-3-(4-methoxyphenyl)-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



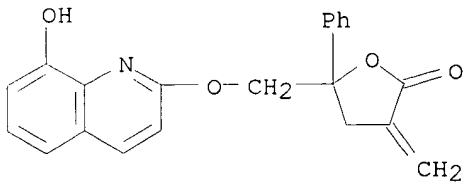
L8 ANSWER 2 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1998:710163 CAPLUS
DN 130:47228
TI Synthesis and anticancer evaluation of certain .gamma.-aryloxymethyl-.alpha.-methylene-.gamma.-phenyl-.gamma.-butyrolactones
AU Wang, Tai-Chi; Lee, Kuan-Han; Chen, Yeh-Long; Liou, Shorong-Shii; Tzeng, Cherng-Chyi
CS School of Chemistry, Kaohsiung Medical College, Taichung, 807, Taiwan
SO Bioorg. Med. Chem. Lett. (1998), 8(19), 2773-2776
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Certain .gamma.-aryloxymethyl-.alpha.-methylene-.gamma.-phenyl-.gamma.-butyrolactones were synthesized and evaluated for their anticancer activity. These compds. demonstrated a strong growth inhibitory activity against leukemia cell lines but are relatively inactive against non-small cell lung cancers and CNS cancers. The anticancer potency for aryl portion is in an order of quinoline> 8-hydroxyquinoline> 2-methylquinoline>> naphthalene>> benzene.
IT **182413-21-4 193551-93-8 201301-67-9**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(synthesis and anticancer evaluation of .gamma.-aryloxymethyl-.alpha.-methylene-.gamma.-phenyl-.gamma.-butyrolactones)
RN 182413-21-4 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-phenyl-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



RN 193551-93-8 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]-5-phenyl- (9CI) (CA INDEX NAME)



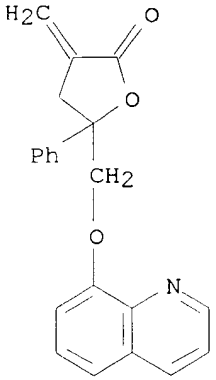
RN 201301-67-9 CAPLUS
CN 2(3H)-Furanone, dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene-5-phenyl- (9CI) (CA INDEX NAME)



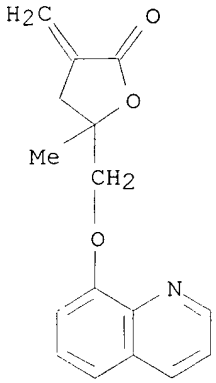
L8 ANSWER 3 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1998:409305 CAPLUS
DN 129:175461
TI .alpha.-Methylene-.gamma.-butyrolactones: synthesis and vasorelaxing activity assay of coumarin, naphthalene, and quinoline derivatives
AU Chen, Yeh-Long; Wang, Tai-Chi; Chang, Nein-Chen; Chang, Ya-Ling; Teng, Che-Ming; Tzeng, Cherng-Chyi
CS School of Chemistry, Kaohsiung Medical College, Kaohsiung, Taiwan
SO Chem. Pharm. Bull. (1998), 46(6), 962-965
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB .alpha.-Methylene-.gamma.-butyrolactone derivs. of coumarin, naphthalene, and quinoline were synthesized and evaluated for vasorelaxing effects on isolated rat thoracic aorta. The 7-[(2,3,4,5-tetrahydro-2-methyl-4-methylene-5-oxo-2-furanyl)methoxy]-2H-1-benzopyran-2-ones, having an aliph. Me substituent at the lactone C2, were more active than their C2-Ph
counterparts against high-K+ (80 mM) medium, Ca2+ (1.9 mM)-induced vasoconstriction and the norepinephrine (NE, 3 .mu.M)-induced phasic and tonic constrictions.
3-Chloro-7-[(2,3,4,5-tetrahydro-2-methyl-4-methylene-5-oxo-2-furanyl)methoxy]-4-methyl-2H-1-benzopyran-2-one demonstrated the most potent inhibitory activities on the NE-induced phasic and tonic constrictions at concns. of as low as 10 .mu.g/mL, and has affinity for both NE-receptor and intrinsic activity to trigger the vasoconstriction. 8-[(2,3,4,5-Tetrahydro-2-methyl-4-methylene-5-oxo-2-furanyl)methoxy]quinoline and other quinoline derivs. are pure irreversible non-competitive blockers of NE-receptor with no intrinsic activity. The arom. ring played an important role in the vasorelaxing effects of .alpha.-methylene-.gamma.-butyrolactones; naphthalene was inactive, quinolines exhibited only affinity to the .alpha.-receptor, and coumarins possessed both affinity and intrinsic activity.

IT **182413-21-4P 182413-22-5P 182413-23-6P**
182413-25-8P 182413-27-0P 182413-28-1P
193551-91-6P 193551-93-8P 193551-95-0P
201301-63-5P 201301-65-7P 201301-66-8P
201301-67-9P 201301-69-1P 201301-70-4P
201301-71-5P 201301-72-6P 211511-06-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and vasorelaxing activity of coumarin, naphthalene, and quinoline derivs. of .alpha.-methylene-.gamma.-butyrolactones)

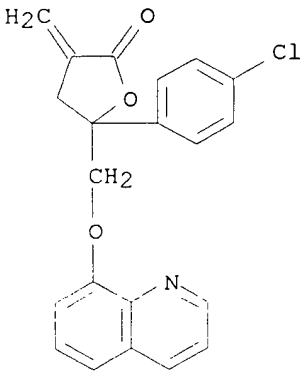
RN 182413-21-4 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-phenyl-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



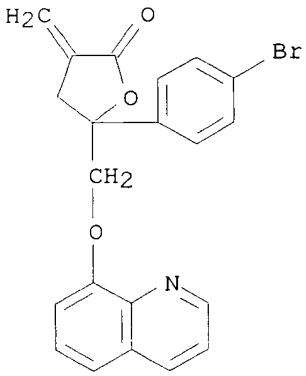
RN 182413-22-5 CAPLUS
CN 2(3H)-Furanone, dihydro-5-methyl-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



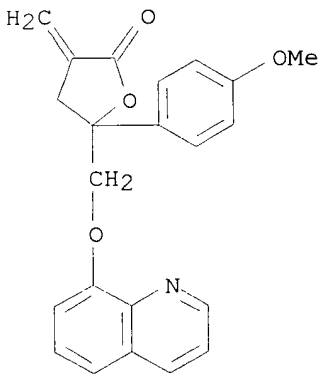
RN 182413-23-6 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



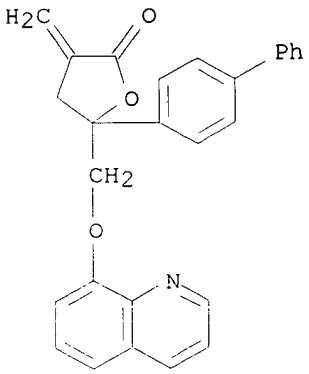
RN 182413-25-8 CAPLUS
CN 2(3H)-Furanone, 5-(4-bromophenyl)dihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



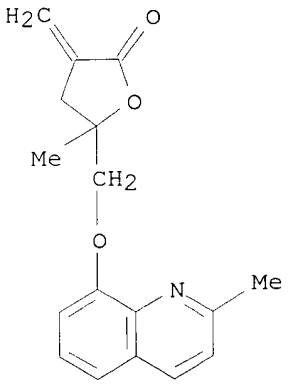
RN 182413-27-0 CAPLUS
CN 2(3H)-Furanone, dihydro-5-(4-methoxyphenyl)-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



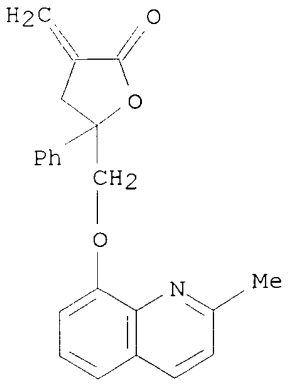
RN 182413-28-1 CAPLUS
CN 2(3H)-Furanone, 5-[1,1'-biphenyl]-4-yldihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



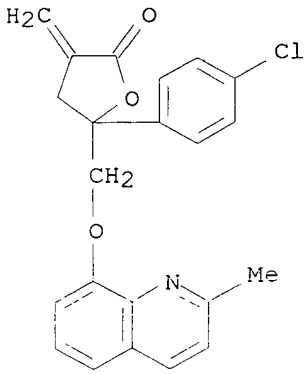
RN 193551-91-6 CAPLUS
CN 2(3H)-Furanone, dihydro-5-methyl-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



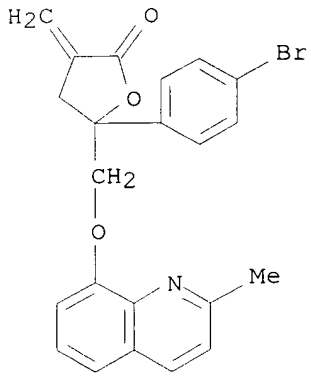
RN 193551-93-8 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]-5-phenyl- (9CI) (CA INDEX NAME)



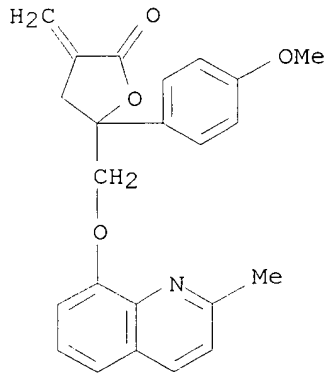
RN 193551-95-0 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



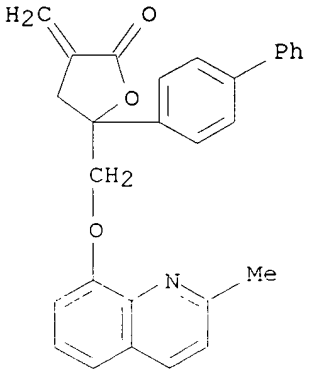
RN 201301-63-5 CAPLUS
CN 2(3H)-Furanone, 5-(4-bromophenyl)dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



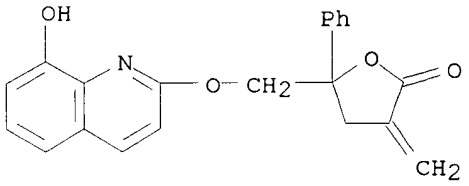
RN 201301-65-7 CAPLUS
CN 2(3H)-Furanone, dihydro-5-(4-methoxyphenyl)-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



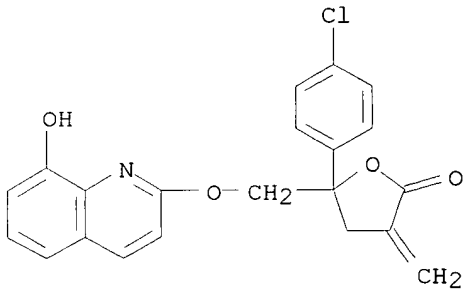
RN 201301-66-8 CAPLUS
CN 2(3H)-Furanone,
5-[1,1'-biphenyl]-4-yldihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



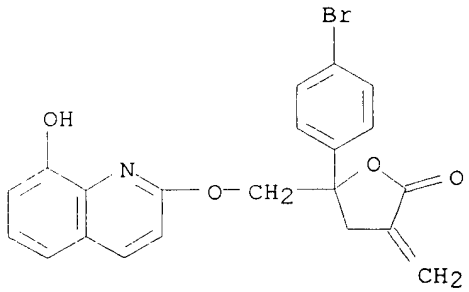
RN 201301-67-9 CAPLUS
CN 2(3H)-Furanone, dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene-5-phenyl- (9CI) (CA INDEX NAME)



RN 201301-69-1 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)

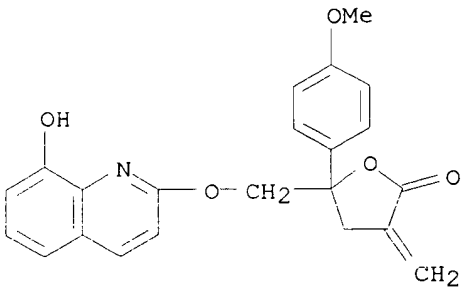


RN 201301-70-4 CAPLUS
CN 2(3H)-Furanone, 5-(4-bromophenyl)dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)

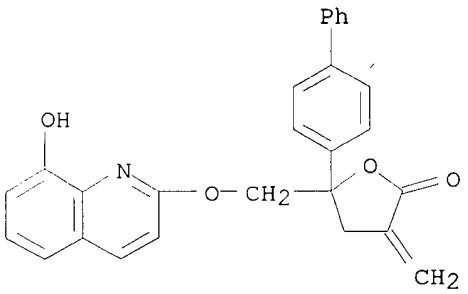


RN 201301-71-5 CAPLUS
CN 2(3H)-Furanone, dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-5-(4-

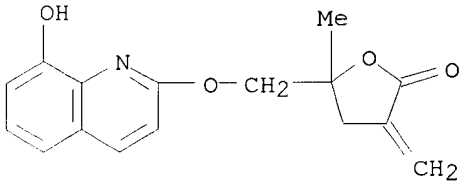
methoxyphenyl)-3-methylene- (9CI) (CA INDEX NAME)



RN 201301-72-6 CAPLUS
CN 2(3H)-Furanone, 5-[1,1'-biphenyl]-4-yldihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)



RN 211511-06-7 CAPLUS
CN 2(3H)-Furanone, dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-5-methyl-3-methylene- (9CI) (CA INDEX NAME)



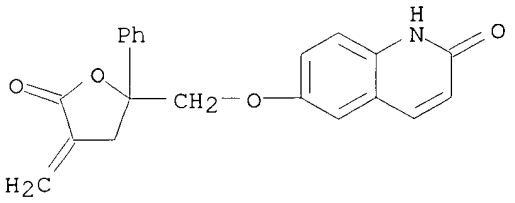
L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1998:408102 CAPLUS
DN 129:136085
TI .alpha.-Methylidene-.gamma.-butyrolactones. Synthesis and evaluation of quinolin-2(1H)-one derivatives
AU Wang, Tai-Chi; Chen, Yeh-Long; Tzeng, Cherng-Chyi; Liou, Shorong-Shii; Tzeng, Weng-Feng; Chang, Ya-Ling; Teng, Che-Ming
CS School Chem., Kaohsiung Med. College, Kaohsiung, 807, Taiwan
SO Helv. Chim. Acta (1998), 81(6), 1038-1047
CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta AG
DT Journal
LA English
OS CASREACT 129:136085
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

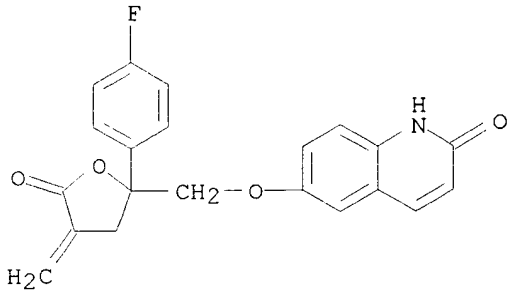
AB As a continuation of previous studies on the synthesis and antiplatelet activity of quinolin-2(1H)-ones with an .alpha.-methylidene-.gamma.-butyrolactone substituted at O(8), O(6)- and N(1)-substituted isomers were synthesized and evaluated for antiplatelet activity against thrombin (Thr)-, arachidonic acid (AA)-, collagen (Col)-, and platelet-activating-factor (PAF)-induced aggregation in washed rabbit platelets. The compds. were synthesized from 6-hydroxyquinolin-2(1H)-one via alkylation and Reformatskii-type condensation. All of them perfectly inhibit AA- and Col-induced platelet aggregation. 6-Substituted isomers I (R = H, F, Cl, Br, MeO, Ph) exhibited very strong inhibitory activities against AA- and PAF-induced aggregation and are .apprx.10 times more potent than their 8-substituted counterparts. However, the 1-substituted and the 1,6-disubstituted counterparts were relatively inactive. Their effects on the Ca2+-dependent vasoconstriction induced by high K+, and the phasic and tonic vasoconstrictions induced by norepinephrine (NE) in rat aorta were also evaluated. Except I (R = Ph), all of them have inhibitory activity on the NE-induced phasic and tonic vasoconstrictions. Compds. II and III also exhibited strong inhibitory activity on high-K+ medium, Ca2+-induced vasoconstriction.

IT **210245-19-5P 210686-70-7P 210686-71-8P**
210686-72-9P 210686-73-0P 210686-74-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and platelet aggregation inhibitory and vasodilating activity of quinolinone-derived methylidene-.gamma.-butyrolactones)

RN 210245-19-5 CAPLUS
CN 2(1H)-Quinolinone, 6-[(tetrahydro-4-methylene-5-oxo-2-phenyl-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)

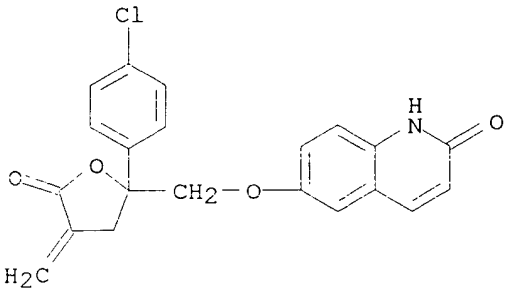


RN 210686-70-7 CAPLUS
CN 2(1H)-Quinolinone, 6-[[2-(4-fluorophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)

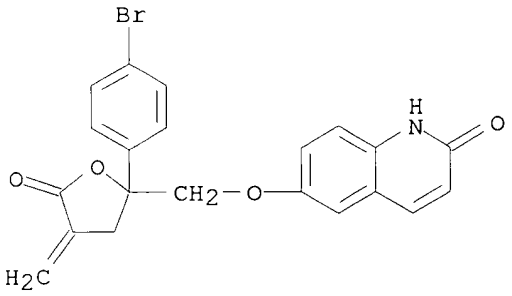


RN 210686-71-8 CAPLUS

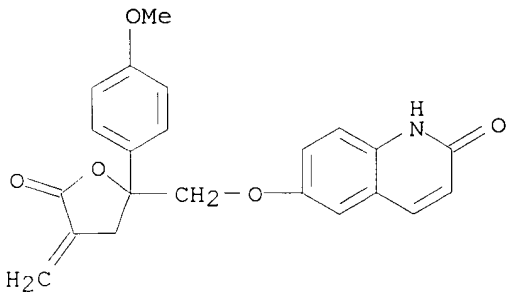
CN 2(1H)-Quinolinone, 6-[[2-(4-chlorophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



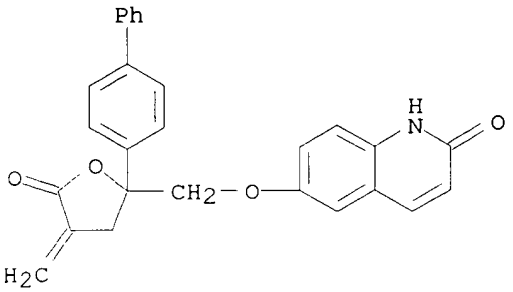
RN 210686-72-9 CAPLUS
CN 2(1H)-Quinolinone, 6-[[2-(4-bromophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



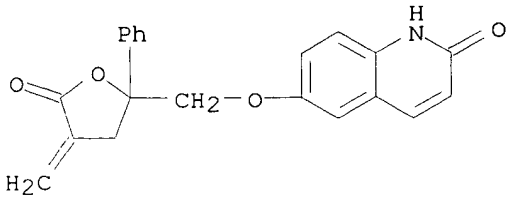
RN 210686-73-0 CAPLUS
CN 2(1H)-Quinolinone,
6-[[tetrahydro-2-(4-methoxyphenyl)-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



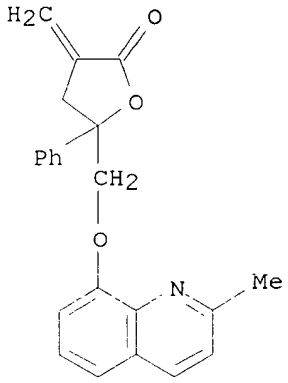
RN 210686-74-1 CAPLUS
CN 2(1H)-Quinolinone,
6-[(2-[1,1'-biphenyl]-4-yltetrahydro-4-methylene-5-oxo-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



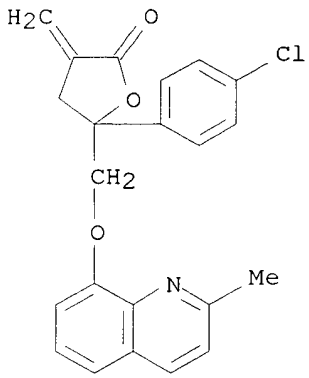
L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1998:343262 CAPLUS
DN 129:117630
TI Cyclic AMP and cyclic GMP phosphodiesterase inhibition by an antiplatelet agent, 6-[(3-methylene-2-oxo-5-phenyl-5-tetrahydrofuranyl)methoxy]quinolinone (CCT-62)
AU Liao, Chang-Hui; Tzeng, Cherng-Chi; Teng, Che-Ming
CS Sect. 1, 1 Jen-Ai Road, College of Medicine, Pharmacological Institute, National Taiwan University, Taipei, Taiwan
SO Eur. J. Pharmacol. (1998), 349(1), 107-114
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB The antiplatelet activity of CCT-62 was detd. in rabbit blood platelets in vitro. CCT-62 inhibited the platelet aggregation and ATP release caused by thrombin (0.1 U/mL), platelet-activating factor (2 ng/mL), collagen (10 .mu.g/mL), arachidonic acid (100 .mu.M), and 9,11-dideoxy-9.alpha.,11.alpha.-methanoepoxy-PGF2.alpha. (1 .mu.M) in a concn.-dependent manner. The IC50 values for platelet aggregation were 18.4.+-.4.5, 10.1.+-.1.6, 3.0.+-.0.9, 1.5.+-.0.3, and 1.0.+-.0.3 .mu.M, resp. CCT-62 also disaggregated the platelets clumped by these aggregation inducers. CCT-62 also inhibited phosphoinositide breakdown and intracellular calcium elevation induced by the platelet aggregation inducers. CCT-62 increased the intracellular cAMP and cGMP levels in a concn.- and time-dependent manner. It potentiated cAMP formation induced by PGE1, but not that caused by 3-isobutyl-1-methylxanthine. CCT-62 did not affect adenylate or guanylate cyclases, but inhibited the cAMP- and cGMP-phosphodiesterase activities. The antiplatelet effect of CCT-62 was reversed by the protein kinase A inhibitor N-[2-(P-bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide (H89). Thus, CCT-62 is an inhibitor of phosphodiesterases and its antiplatelet effects are mediated mainly by elevation of cAMP levels.
IT **210245-19-5**, CCT 62
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cAMP and cGMP phosphodiesterases inhibition in rabbit blood platelets by CCT-62)
RN 210245-19-5 CAPLUS
CN 2(1H)-Quinolinone, 6-[(tetrahydro-4-methylene-5-oxo-2-phenyl-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



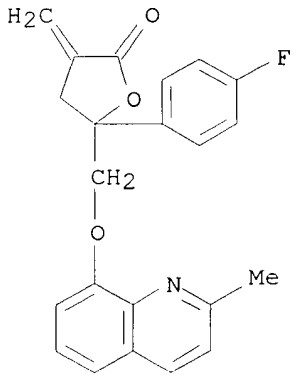
L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1997:771563 CAPLUS
DN 128:97501
TI Synthesis and antiplatelet evaluation of .alpha.-methylene-.gamma.-butyrolactone bearing 2-methylquinoline and 8-hydroxyquinoline moieties
AU Liou, Shorong-Shii; Zhao, Yue-Ling; Chang, Ya-Ling; Teng, Che-Ming; Tzeng, Cherng-Chyi
CS Department of Pharmacy, Tajen Junior College of Pharmacy, Pingtung, Taiwan
SO Chem. Pharm. Bull. (1997), 45(11), 1777-1781
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB In a search for inhibitors of platelet aggregation, some .alpha.-methylene-.gamma.-butyrolactones bearing 2-methylquinoline and 8-hydroxyquinoline moieties were synthesized and evaluated for antiplatelet activities against thrombin (Thr)-, arachidonic acid (AA)-, collagen (Col)-, and platelet-activating factor (PAF)- induced aggregation in washed rabbit platelets. With the exception of 2-[[2,3,4,5-tetrahydro-4-methylene-5-oxo-2-(4-phenylphenyl)-2-furanyl]methoxy]-8-hydroxyquinoline (8f), these .alpha.-methylene-.gamma.-butyrolactones completely inhibited the platelet aggregation induced by AA and Col. The 2-methylquinoline derivs. were also active against Thr- and PAF-induced aggregation, while their 8-hydroxyquinoline counterparts were relatively inactive.
IT **193551-93-8P 193551-95-0P 201301-62-4P**
201301-63-5P 201301-65-7P 201301-66-8P
201301-67-9P 201301-68-0P 201301-69-1P
201301-70-4P 201301-71-5P 201301-72-6P
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antiplatelet activity of .alpha.-methylene-.gamma.-butyrolactone bearing 2-methylquinoline and 8-hydroxyquinoline moieties)
RN 193551-93-8 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]-5-phenyl- (9CI) (CA INDEX NAME)



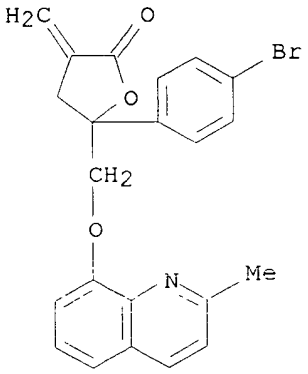
RN 193551-95-0 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



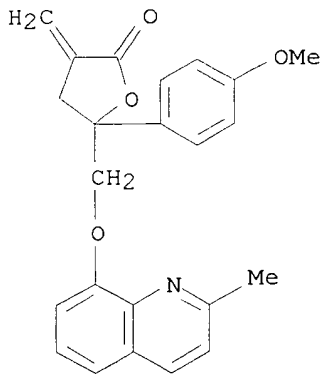
RN 201301-62-4 CAPLUS
CN 2(3H)-Furanone, 5-(4-fluorophenyl)dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



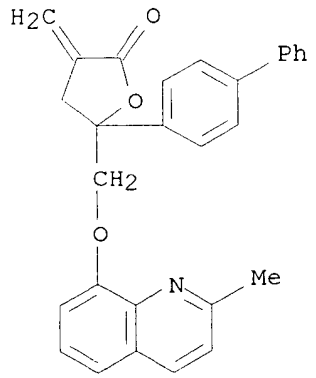
RN 201301-63-5 CAPLUS
CN 2(3H)-Furanone, 5-(4-bromophenyl)dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



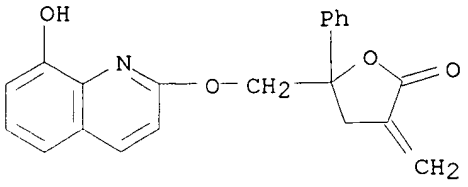
RN 201301-65-7 CAPLUS
CN 2(3H)-Furanone, dihydro-5-(4-methoxyphenyl)-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



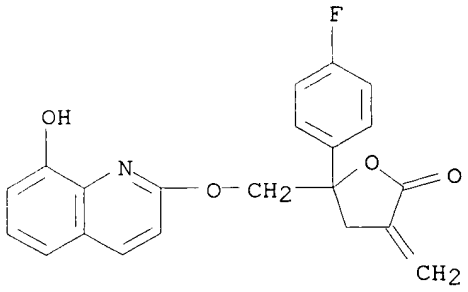
RN 201301-66-8 CAPLUS
CN 2(3H)-Furanone,
5-[1,1'-biphenyl]-4-yldihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



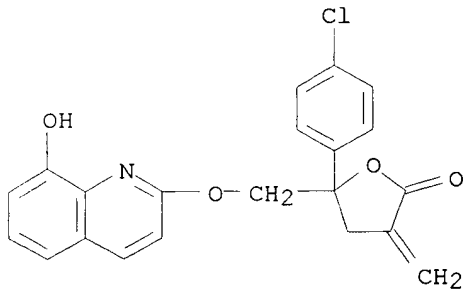
RN 201301-67-9 CAPLUS
CN 2(3H)-Furanone, dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene-5-phenyl- (9CI) (CA INDEX NAME)



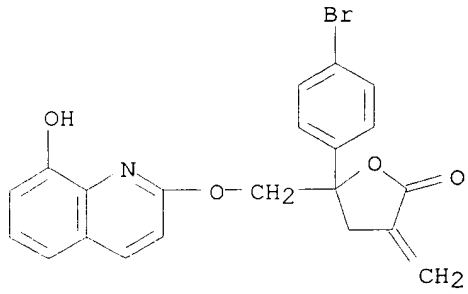
RN 201301-68-0 CAPLUS
CN 2(3H)-Furanone, 5-(4-fluorophenyl)dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)



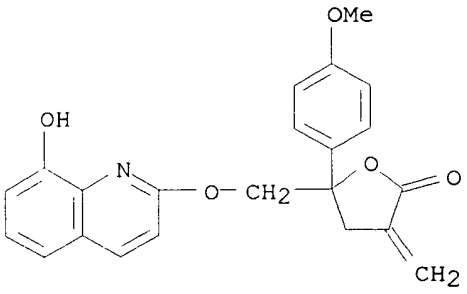
RN 201301-69-1 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)



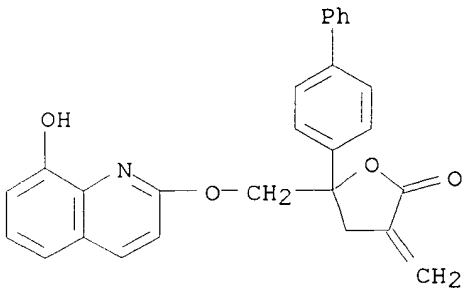
RN 201301-70-4 CAPLUS
CN 2(3H)-Furanone, 5-(4-bromophenyl)dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)



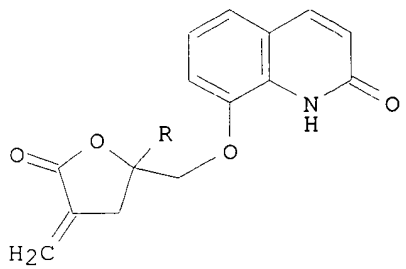
RN 201301-71-5 CAPLUS
CN 2(3H)-Furanone, dihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-5-(4-methoxyphenyl)-3-methylene- (9CI) (CA INDEX NAME)



RN 201301-72-6 CAPLUS
CN 2(3H)-Furanone, 5-[1,1'-biphenyl]-4-yldihydro-5-[[(8-hydroxy-2-quinolinyl)oxy]methyl]-3-methylene- (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1997:461309 CAPLUS
DN 127:161686
TI Synthesis and evaluation of 2-{[(2-oxo-1H-quinolin-8-yl)oxy]methyl}-substituted .alpha.-methylidene-.gamma.-butyrolactones
AU Tzeng, Cherng Chyi; Chen, Yeh Long; Wang, Chyi Jia; Wang, Tai Chi; Chang, Ya Ling; Teng, Che Ming
CS School Chemistry, Kaohsiung Medical College, Kaohsiung, 807, Taiwan
SO Helv. Chim. Acta (1997), 80(4), 1161-1168
CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta
DT Journal
LA English
OS CASREACT 127:161686
GI



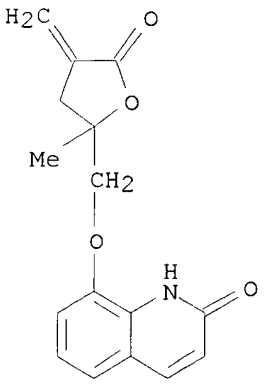
I

AB O-alkylation of 8-hydroxy-1H-quinolin-2-one afforded 8-(2-oxopropoxy)-1H-quinolin-2-one which was immediately cyclized to form the tricyclic 2,3-dihydro-3-hydroxy-3-methyl-5H-pyrido[1,2,3-de][1,4]benzoxazine-5-one. Reformatsky-type condensation of the latter furnished platelet aggregation

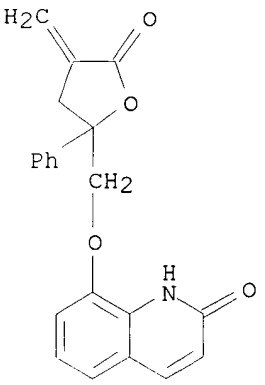
inhibitor (furanylmethoxy)quinolinone I (R = Me). Its counterparts I (R =
4-R1C6H4; R1 = H, F, Cl, Br, Ph, MeO, NO2) were obtained from 8-hydroxy-1H-quinolin-2-one via alkylation and Reformatsky-type condensation. Although I (R = Me) was less active against platelet aggregation than I (R = 4-R1C6H4), it was the only compd. which exhibited significant inhibitory activity on high-K+ medium, Ca2+-induced vasoconstriction and was more active than most of its Ph-substituted counterparts against norepinephrine-induced vasoconstrictions.

IT **193551-84-7P 193551-86-9P 193821-81-7P**
193821-82-8P 193821-83-9P 193821-84-0P
193821-85-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of quinolinones as platelet aggregation inhibitors and vasodilators)

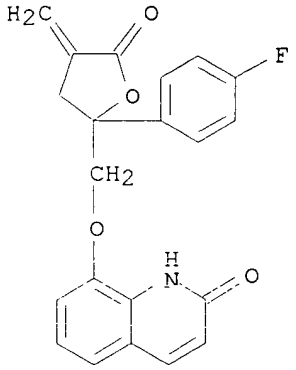
RN 193551-84-7 CAPLUS
CN 2(1H)-Quinolinone, 8-[(tetrahydro-2-methyl-4-methylene-5-oxo-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



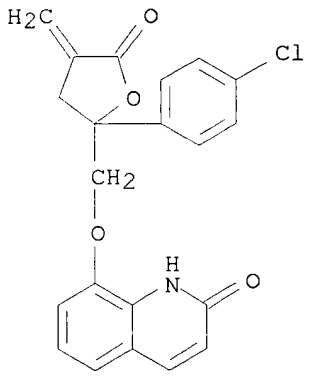
RN 193551-86-9 CAPLUS
CN 2(1H)-Quinolinone, 8-[(tetrahydro-4-methylene-5-oxo-2-phenyl-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



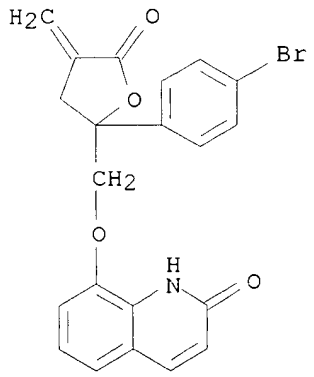
RN 193821-81-7 CAPLUS
CN 2(1H)-Quinolinone, 8-[[2-(4-fluorophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



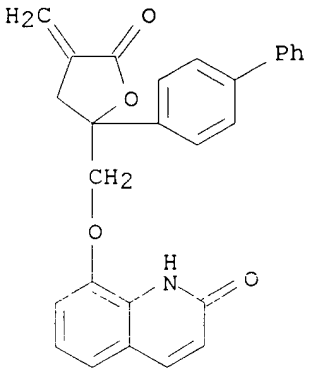
RN 193821-82-8 CAPLUS
CN 2(1H)-Quinolinone, 8-[[2-(4-chlorophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



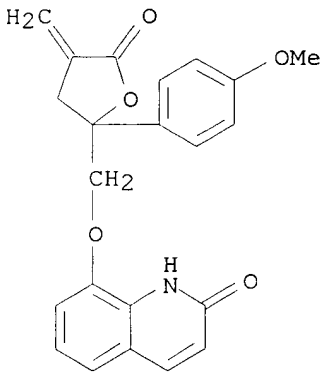
RN 193821-83-9 CAPLUS
CN 2(1H)-Quinolinone, 8-[[2-(4-bromophenyl)tetrahydro-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



RN 193821-84-0 CAPLUS
CN 2(1H)-Quinolinone,
8-[(2-[1,1'-biphenyl]-4-yltetrahydro-4-methylene-5-oxo-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



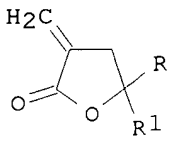
RN 193821-85-1 CAPLUS
CN 2(1H)-Quinolinone,
8-[[tetrahydro-2-(4-methoxyphenyl)-4-methylene-5-oxo-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)



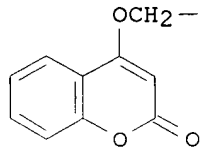
L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1997:456149 CAPLUS
DN 127:161700
TI Preparation of .alpha.-methylene-.gamma.-butyrolactones as new inhibitors of platelet aggregation
IN Tzeng, Cherng-chyi; Chen, Yeh-long; Wang, Tai-chi; Teng, Che-ming
PA National Science Council, Taiwan
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5646164	A	19970708	US 1995-557268	19951114

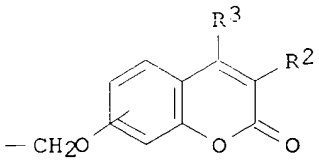
OS MARPAT 127:161700
GI



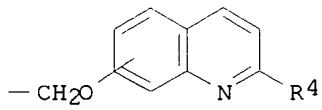
I



II



III



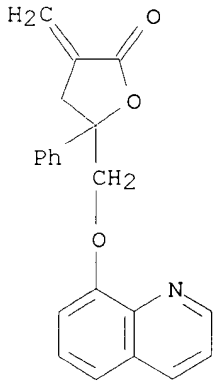
IV

AB The title compds. [I; R = II, III, IV (wherein R2 = H, halo, C1-4 alkyl, etc.; R3 = H, halo, Ph, etc.; R4 = H, OH, C1-4 alkyl); R1 = Me, (un)substituted Ph], potent inhibitors of platelet aggregation and therefore useful in the treatment or the prevention of cardiovascular disease, were prepd. Thus, reacting 4-hydroxycoumarin with chloroacetone in the presence of K2CO3 in Me2CO followed by reaction of the resulting 4-(2-oxopropoxy)-2H-1-benzopyran-2-one with Et 2-(bromomethyl)acrylate in the presence of Zn and hydroquinone in THF afforded I [R = II; R1 = Me] which showed IC50 of >50 .mu.g/mL against platelet aggregation induced, e.g., by thrombin.

IT **182413-21-4P 182413-22-5P 182413-23-6P**
193551-84-7P 193551-86-9P 193551-91-6P
193551-93-8P 193551-95-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .alpha.-methylene-.gamma.-butyrolactones as new inhibitors of platelet aggregation)

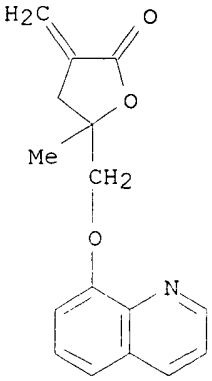
RN 182413-21-4 CAPLUS

CN 2(3H)-Furanone, dihydro-3-methylene-5-phenyl-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)

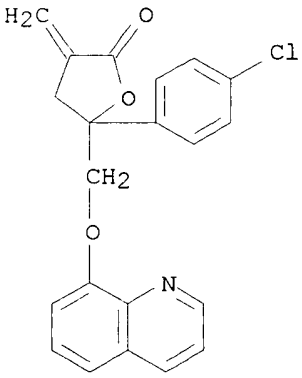


RN 182413-22-5 CAPLUS

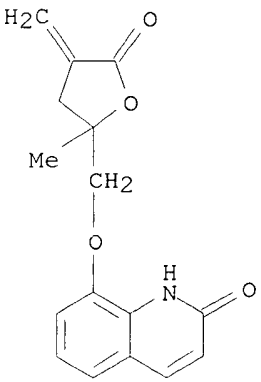
CN 2(3H)-Furanone, dihydro-5-methyl-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



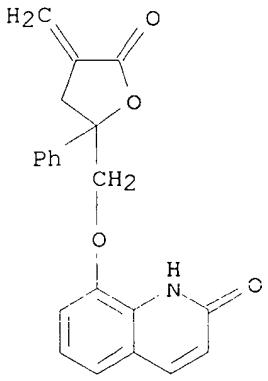
RN 182413-23-6 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



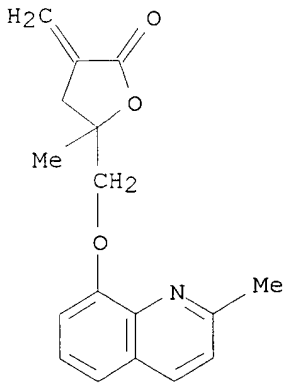
RN 193551-84-7 CAPLUS
CN 2(1H)-Quinolinone, 8-[(tetrahydro-2-methyl-4-methylene-5-oxo-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



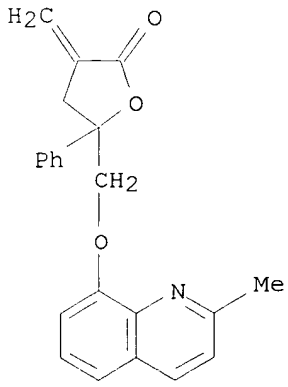
RN 193551-86-9 CAPLUS
CN 2(1H)-Quinolinone, 8-[(tetrahydro-4-methylene-5-oxo-2-phenyl-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)



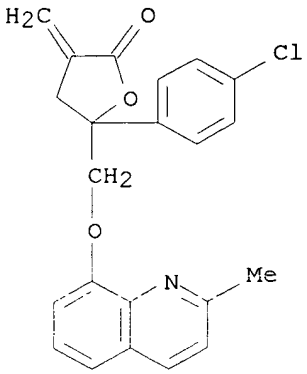
RN 193551-91-6 CAPLUS
CN 2(3H)-Furanone, dihydro-5-methyl-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



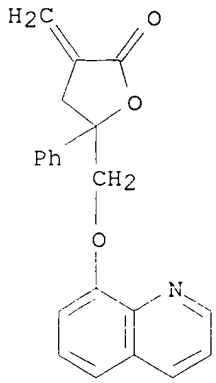
RN 193551-93-8 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]-5-phenyl- (9CI) (CA INDEX NAME)



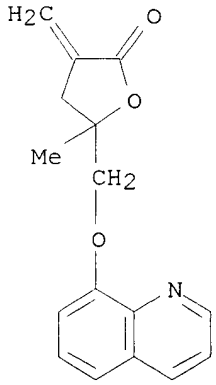
RN 193551-95-0 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-3-methylene-5-[[(2-methyl-8-quinolinyl)oxy]methyl]- (9CI) (CA INDEX NAME)



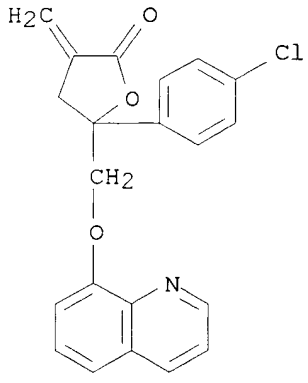
L8 ANSWER 9 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1996:616042 CAPLUS
DN 125:275458
TI Antiplatelet .alpha.-methylidene-.gamma.-butyrolactones. Synthesis and evaluation of quinoline, flavone, and xanthone derivatives
AU Wang, Tai Chi; Chen, Yeh Long; Tzeng, Cherng Chyi; Liou, Shorong Shii; Chang, Ya Ling; Teng, Che Ming
CS School Chem., Kaohsiung Medical College, Kaohsiung, Taiwan
SO Helv. Chim. Acta (1996), 79(6), 1620-1626
CODEN: HCACAV; ISSN: 0018-019X
DT Journal
LA English
AB As a continuation of our previous studies on the synthesis and antiplatelet activity of coumarin derivs. of .alpha.-methylidene-.gamma.-butyrolactones, quinoline, flavone, and xanthone derivs. were prepd. and evaluated for antiplatelet activity against thrombin-, arachidonic acid-(AA), collagen, and platelet-activating factor-induced aggregation in washed rabbit platelets. The compds. were prepd. from 8-quinolinol, 7-flavonol, and 3-xanthonol, resp., via alkylation and Reformatsky-type condensation. By the comparison with coumarin .alpha.-methylidene-.gamma.-butyrolactone, flavone and xanthone derivs. are more selective in which only AA- and collagen-induced aggregation are strongly inhibited. Most of the quinoline derivs. exhibited broad spectrum antiplatelet activities.
IT **182413-21-4P 182413-22-5P 182413-23-6P 182413-25-8P 182413-27-0P 182413-28-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of methylidenebutyrolactones derived. from quinolines, flavones, and xanthones as blood platelet aggregation inhibitors)
RN 182413-21-4 CAPLUS
CN 2(3H)-Furanone, dihydro-3-methylene-5-phenyl-5-[(8-quinolinyloxy)methyl]-(9CI) (CA INDEX NAME)



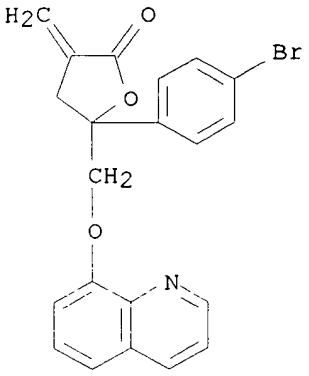
RN 182413-22-5 CAPLUS
CN 2(3H)-Furanone, dihydro-5-methyl-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



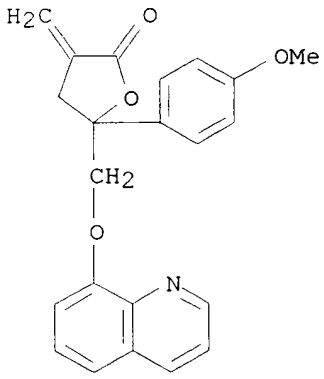
RN 182413-23-6 CAPLUS
CN 2(3H)-Furanone, 5-(4-chlorophenyl)dihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



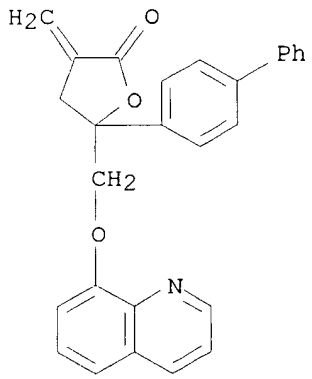
RN 182413-25-8 CAPLUS
CN 2(3H)-Furanone, 5-(4-bromophenyl)dihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



RN 182413-27-0 CAPLUS
CN 2(3H)-Furanone, dihydro-5-(4-methoxyphenyl)-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)



RN 182413-28-1 CAPLUS
CN 2(3H)-Furanone, 5-[1,1'-biphenyl]-4-yldihydro-3-methylene-5-[(8-quinolinyloxy)methyl]- (9CI) (CA INDEX NAME)

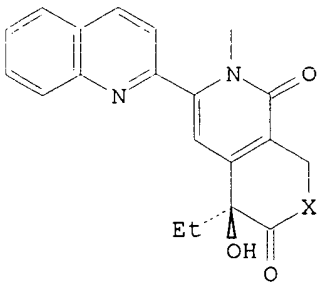


L8 ANSWER 10 OF 10 CAPLUS COPYRIGHT 1999 ACS
AN 1989:115161 CAPLUS
DN 110:115161
TI Modification of the hydroxylactone ring of camptothecin: inhibition of mammalian topoisomerase I and biological activity
AU Hertzberg, Robert P.; Caranfa, Mary Jo; Holden, Kenneth G.; Jakas, Dalia R.; Gallagher, Gregory; Mattern, Michael R.; Mong, Shau Ming; Bartus, Joan
O'Leary; Johnson, Randall K.; Kingsbury, William D.

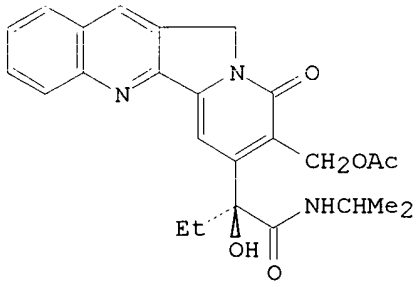
CS Dep. Med. Chem., Smith Kline and French Lab., King of Prussia, PA, 19406, USA

SO J. Med. Chem. (1989), 32(3), 715-20
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 110:115161

GI



I



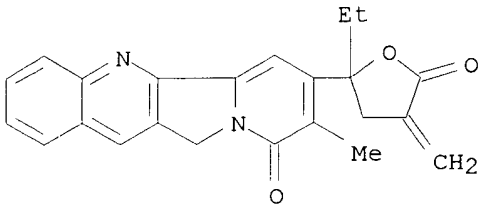
II

AB Several camptothecin (I, X = O) derivs. contg. a modified hydroxy lactone ring, e.g. I (X = NH, NCHMe2, S) were synthesized and evaluated for inhibition of topoisomerase I and cytotoxicity to mammalian cells. Thus, the comptothecin carbinolamide deriv. II was treated with NaN3 followed by catalytic redn. and thermal cyclization to give I (X = NH). Each of the groups of the hydroxy lactone moiety, the carbonyl oxygen, the ring lactone oxygen, and the 20-hydroxy group, were shown to be crit. for enzyme inhibition. The compds. that did not inhibit topoisomerase I were not cytotoxic to mammalian cells. One of these compds. was tested for antitumor activity and was found to be inactive. The hydroxy lactone ring of camptothecin is crit. for antitumor activity in vivo.

IT **118514-68-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., topoisomerase I inhibition, and cytotoxic activity of)

RN 118514-68-4 CAPLUS

CN Indolizino[1,2-b]quinolin-9(11H)-one, 7-(2-ethyltetrahydro-4-methylene-5-oxo-2-furanyl)-8-methyl- (9CI) (CA INDEX NAME)



WEST

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Search Results -

Term	Documents
PRIMAQUINE.DWPI,EPAB,JPAB.	62
PRIMAQUINES	0
PRIMAQUINE.JPAB,EPAB,DWPI.	62

Database: All Foreign Patents Abstracts Databases (JPAB + EPAB + DWPI)

Refine Search: primaquine

Search History

DB Name	Query	Hit Count	Set Name
JPAB,EPAB,DWPI	primaquine	62	L5
JPAB,EPAB,DWPI	gametocytocidal	1	L4
JPAB,EPAB,DWPI	primaquine and gametocytocid$	0	L3
USPT	l1 and gametocytocidal	1	L2
USPT	primaquine	217	L1

Document Number 1

Entry 1 of 1 File: USPT May 5, 1998

DOCUMENT-IDENTIFIER: US 5747476 A
TITLE: Treatment of equine protozoal myeloencephalitis

BSPR:
The gametocytocidal and sporontocidal effects of 2 g sulfadiazine with 50 mg pyrimethamine in a chloroquine-resistant strain of Plasmodium falciparum is disclosed in Chemical Abstracts, Volume 69: 50900p (1968). Primaquine diphosphate, pyrimethamine and sulfadiazine were said to show causal prophylactic activity against rodent malaria, Plasmodium berghei yoelii, as disclosed in Chemical Abstracts, Volume 77: 109339h (1972). A three component composition of pyrimethamine, sulfadiazine and cycloguanil-HCl for treating rodent malaria is disclosed in Chemical Abstracts, Volume 96: 40845t (1982). Similarly, sulfadiazine sodium has been used to enhance the activities of certain antiinfective drugs against infections caused by pyrimethamine-susceptible or pyrimethamine-resistant strains of P. falciparum and P. vivax in owl monkeys. See, Chemical Abstracts, Volume 92: 15581p (1980).

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 INDEX 'ADISALERTS, ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, AQUASCI,
     BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, CABA,
CANCERLIT,
     CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
DRUGB,
     DRUGLAUNCH, DRUGMONOG2, DRUGNL, ...' ENTERED AT 12:40:22 ON 29 OCT 1999
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                1   FILE ANABSTR
               15   FILE BIOSIS
               12   FILE CABA
                2   FILE CANCERLIT
                9   FILE CAPLUS
                3   FILE DDFB
               10   FILE DDFU
                3   FILE DRUGB
               14   FILE DRUGU
               16   FILE EMBASE
                1   FILE ESBIOBASE
                6   FILE LIFESCI
               16   FILE MEDLINE
                5   FILE NTIS
                1   FILE PROMT
                8   FILE SCISEARCH
                4   FILE TOXLINE
                6   FILE TOXLIT
                1   FILE USPATFULL
L14              QUE PRIMAQUINE AND GAMETOCYTOCIDAL
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     FILE 'MEDLINE, EMBASE' ENTERED AT 12:41:28 ON 29 OCT 1999
L15           32 S L14
L16            1 S L14 AND REVIEW/DT
L17            4 S L14 AND REVIEW?
L18            4 S L17 NOT L16
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L18 ANSWER 1 OF 4 MEDLINE
AN 95397605 MEDLINE
DN 95397605
TI Malaria treatment in Vanuatu: new national treatment guidelines.
AU Reeve P A
CS Vila Central Hospital, Vanuatu.
SO PAPUA NEW GUINEA MEDICAL JOURNAL, (1994 Sep) 37 (3) 181-8.
Journal code: YEU. ISSN: 0031-1480.
CY Papua New Guinea
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199512
AB In Vanuatu malaria is a major killer, especially of young children. As most deaths occur outside the hospital it is very important to have simple, clear guidelines on the management of patients with suspected malaria for the primary health care workers who treat the majority of cases. Despite the encouragement of early treatment, malaria was the major cause of death in children after the neonatal period in 1988. During 1989 and 1990 the treatment of malaria in Vanuatu was **reviewed** with the aim of trying to reduce the morbidity and mortality from the disease. New guidelines were included in the Vanuatu Health Workers' Manual, issued to all nurses, nurse practitioners and doctors in 1991. The major changes were the introduction of immediate slide microscopy, the use of a combination of chloroquine and sulphadoxine-pyrimethamine for Plasmodium falciparum malaria and for children under 5 years and pregnant women, the discontinuation of single-dose **primaquine** (previously given as a **gametocytocidal** agent), and the use of a loading dose of quinine. The constraints of the previous guidelines, the rationale for the changes and the expected improvements resulting from using the new treatments are discussed.

L18 ANSWER 2 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97304426 EMBASE
DN 1997304426
TI Antimalarial drugs and the mosquito transmission of Plasmodium.
AU Butcher G.A.
CS G.A. Butcher, Department of Biology, Imperial College of Science, Technology and Medicine, Prince Consort Road, London SW7 2BB, United Kingdom. g.butche@ic.ac.uk
SO International Journal for Parasitology, (1997) 27/9 (975-987).
Refs: 114
ISSN: 0020-7519 CODEN: IJPYBT
PUI S 0020-7519(97)00079-9
CY United Kingdom
DT Journal; General Review
FS 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LA English
SL English
AB It is well-known that whenever possible, the treatment of patients with malaria should include measures to prevent them transmitting the infection to others. This is particularly important for P. falciparum, where the gametocytes can survive for a much longer period than the asexual stages.

Not all antimalarials are **gametocytocidal** or sporontocidal and those that are may have particular disadvantages or lose their effectiveness because of resistance. Even drugs that have no obvious **gametocytocidal** or sporontocidal activity may have other effects. These include the possibility of increasing transmission, either by affecting the parasite within an individual host or by selection for parasite strains with increased potential for infecting the mosquito vector. This **review** summarises the available information on the properties of antimalarials in relation to mosquito transmission and highlights the need for more attention to be paid to this aspect of drug action.

L18 ANSWER 3 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96295735 EMBASE
DN 1996295735
TI **Primaquine** resistance in Plasmodium vivax.
AU Collins W.E.; Jeffery G.M.
CS Division of Parasitic Diseases, Ctrs. for Disease Control/Prevention, 4770
Buford Highway,Atlanta, GA 30341, United States
SO American Journal of Tropical Medicine and Hygiene, (1996) 55/3 (243-249).
ISSN: 0002-9637 CODEN: AJTHAB
CY United States
DT Journal; General Review
FS 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Reports have appeared calling attention to what has been termed **primaquine** resistance in Plasmodium vivax in several geographic areas. The possibility exists that **primaquine** tolerant strains (often referred to as the tropical zone type from the South Pacific and Southeast Asian regions characterized by early and frequent relapses) may have become widely disseminated to areas where they had not previously existed through the widespread population mobility that has characterized the last 50 years. The appearance in the relatively recent past of strains of P. vivax, particularly from the South Pacific area, that are resistant to the 4-aminoquinolines has added a new dimension to the resistance problem. While there seems to be little evidence to date of the existence of acquired **primaquine** resistance in P. vivax, the possibility of its emergence in the future can certainly not be ruled out, and its timely detection and confirmation will be most important, albeit quite difficult because of the relatively covert sites of drug effect. The occurrence of relapses in P. vivax after **primaquine** therapy would be assumed to be the most reliable indication of resistance. Reports of the sporontocidal or **gametocytocidal** activity of **primaquine** when used alone (i.e., without concomitant administration of an effective suppressive) against a P. vivax infection have been few and inconclusive. The establishment of baselines of this activity in P. vivax might be useful in detecting and evaluating **primaquine** resistance in this species.

L18 ANSWER 4 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 81248762 EMBASE
DN 1981248762
TI Clinical problems associated with the use of **primaquine** as a tissue schizontocidal and **gametocytocidal** drug.
AU Clyde D.F.
CS WHO Reg. Off. South East Asia, New Delhi 110002, India
SO Bulletin of the World Health Organization, (1981) 59/3 (391-395).
CODEN: BWHOA6

CY Switzerland
DT Journal
FS 004 Microbiology
038 Adverse Reactions Titles
037 Drug Literature Index
030 Pharmacology
LA English
SL French
AB Clinically important side-effects of **primaquine** are **reviewed**. These include gastrointestinal disturbances, methemoglobinemia, acute intravascular hemolysis in individuals deficient in glucose-6-phosphate dehydrogenase (G6PD), and possibly immunosuppression through inhibition of lymphocyte proliferation. Dosages of 30 or 45 mg (base) of **primaquine**, given at weekly intervals, are suitable for patients with G6PD deficiency. If possible, **primaquine** should not be administered until the acute symptoms of the malaria attack have been brought under control.